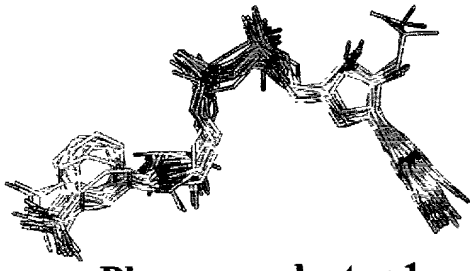
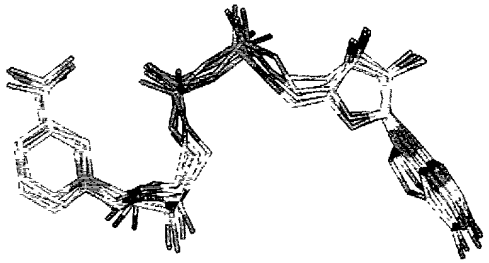
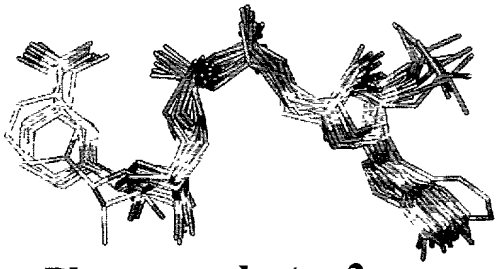
Dehydrogenase Pharmacoclusters



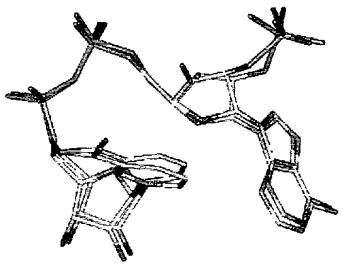
Pharmacocluster 1



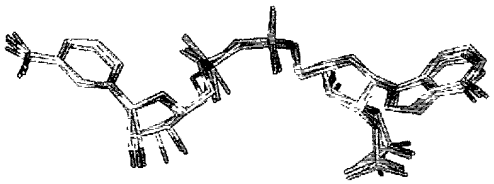
Pharmacocluster 2



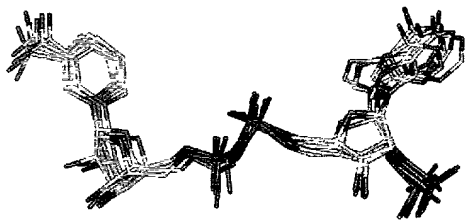
Pharmacocluster 3



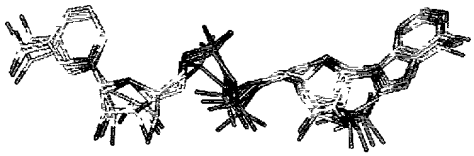
Pharmacocluster 4



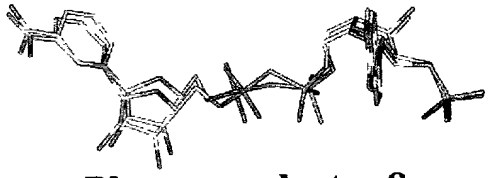
Pharmacocluster 5



Pharmacocluster 6



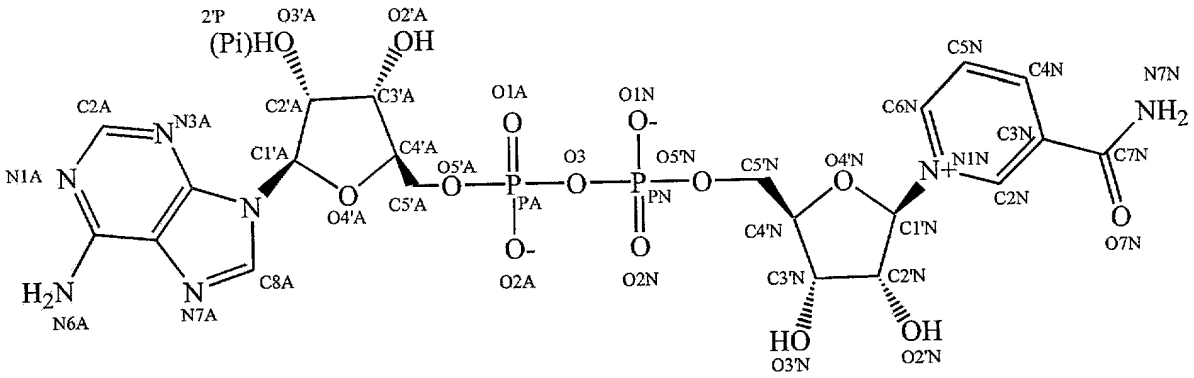
Pharmacocluster 7



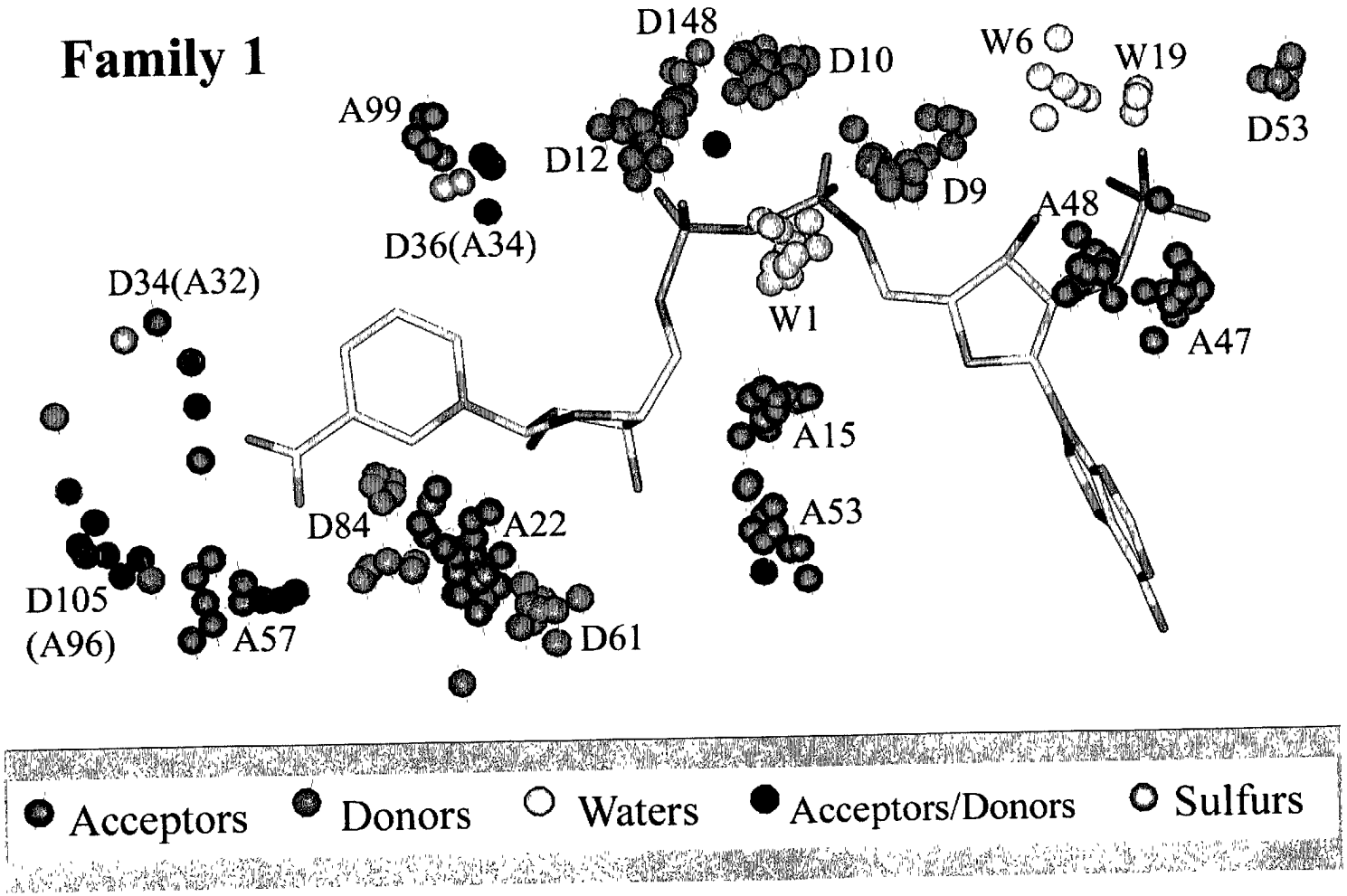
Pharmacocluster 8

EDO4080855.4.02.2001

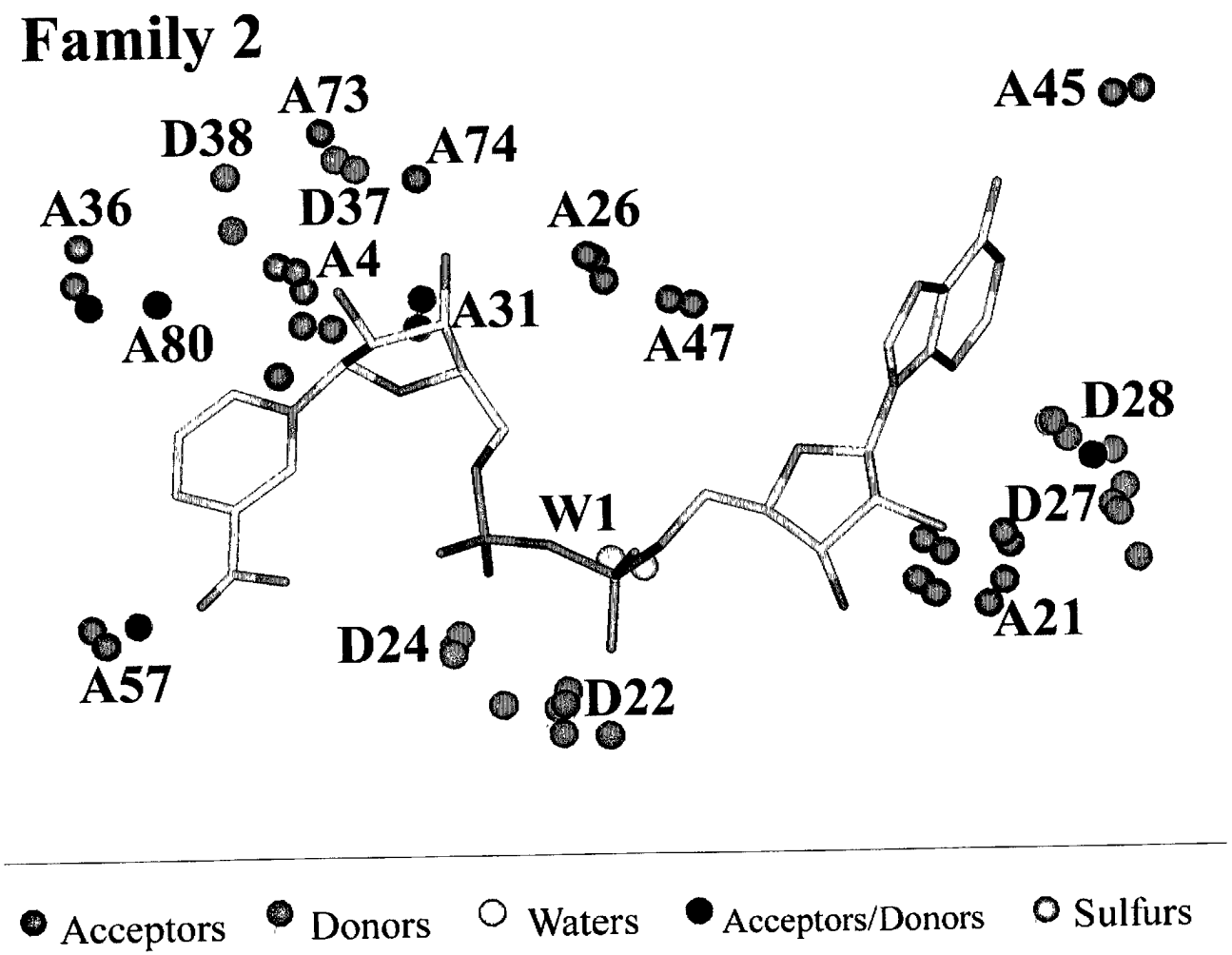
Sem et al.
P-TB 5072
Figure 2



T0822T 5680n00T

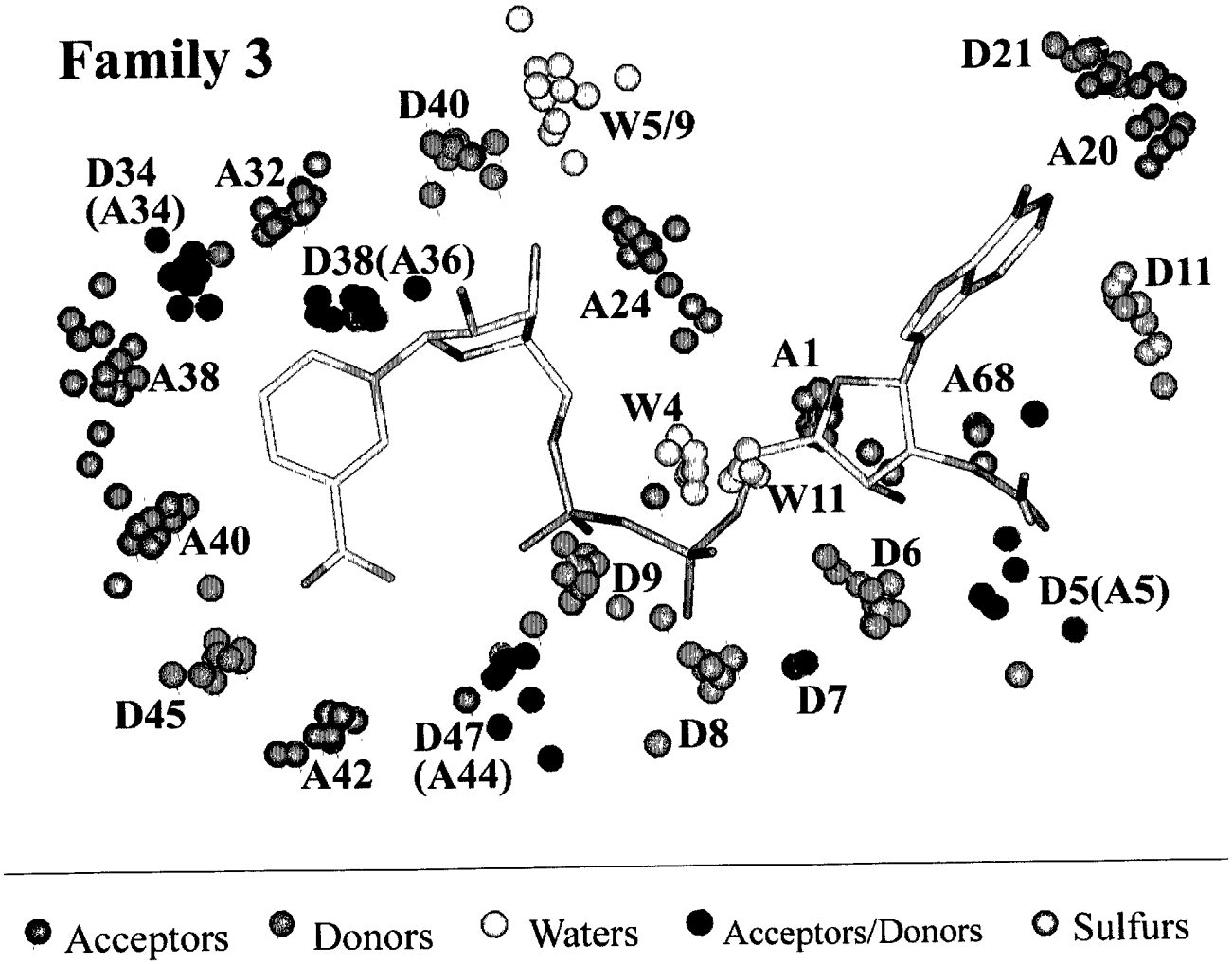


Sem et al.
P-TB 5072
Figure 3A



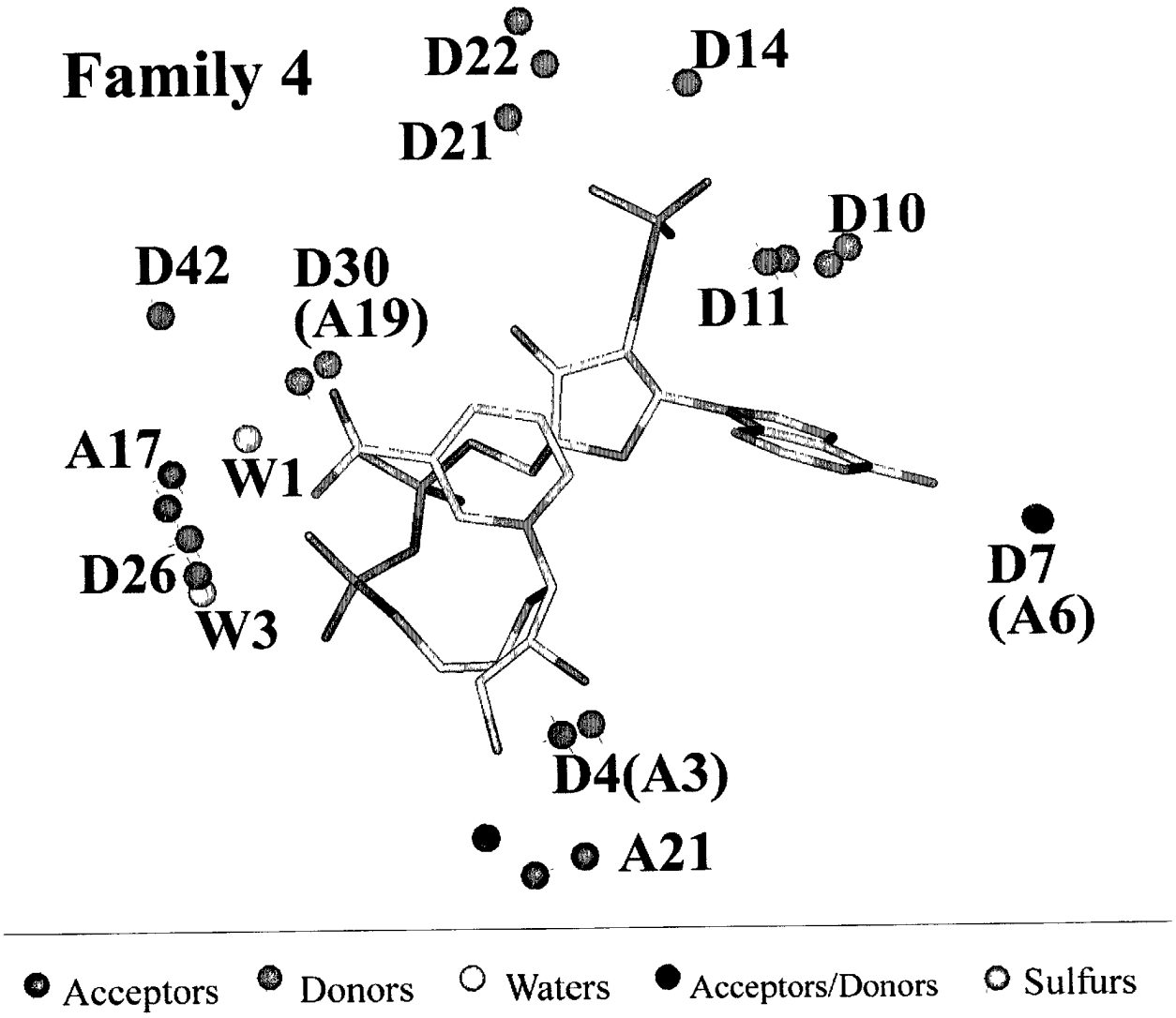
Sem et al.
P-TB 5072
Figure 3B

T0822F 5680n00T

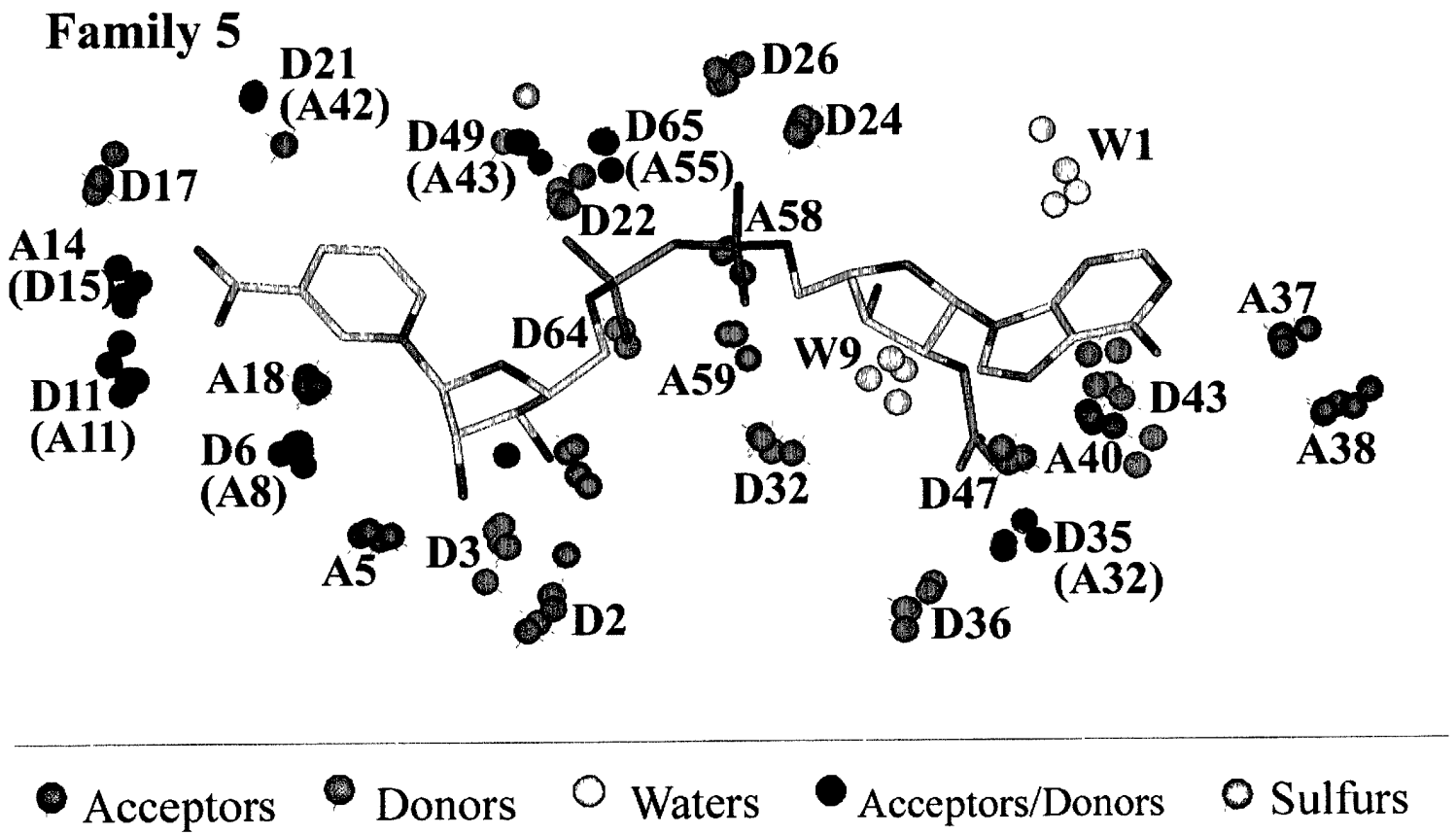


Sem et al.
P-TB 5072
Figure 3C

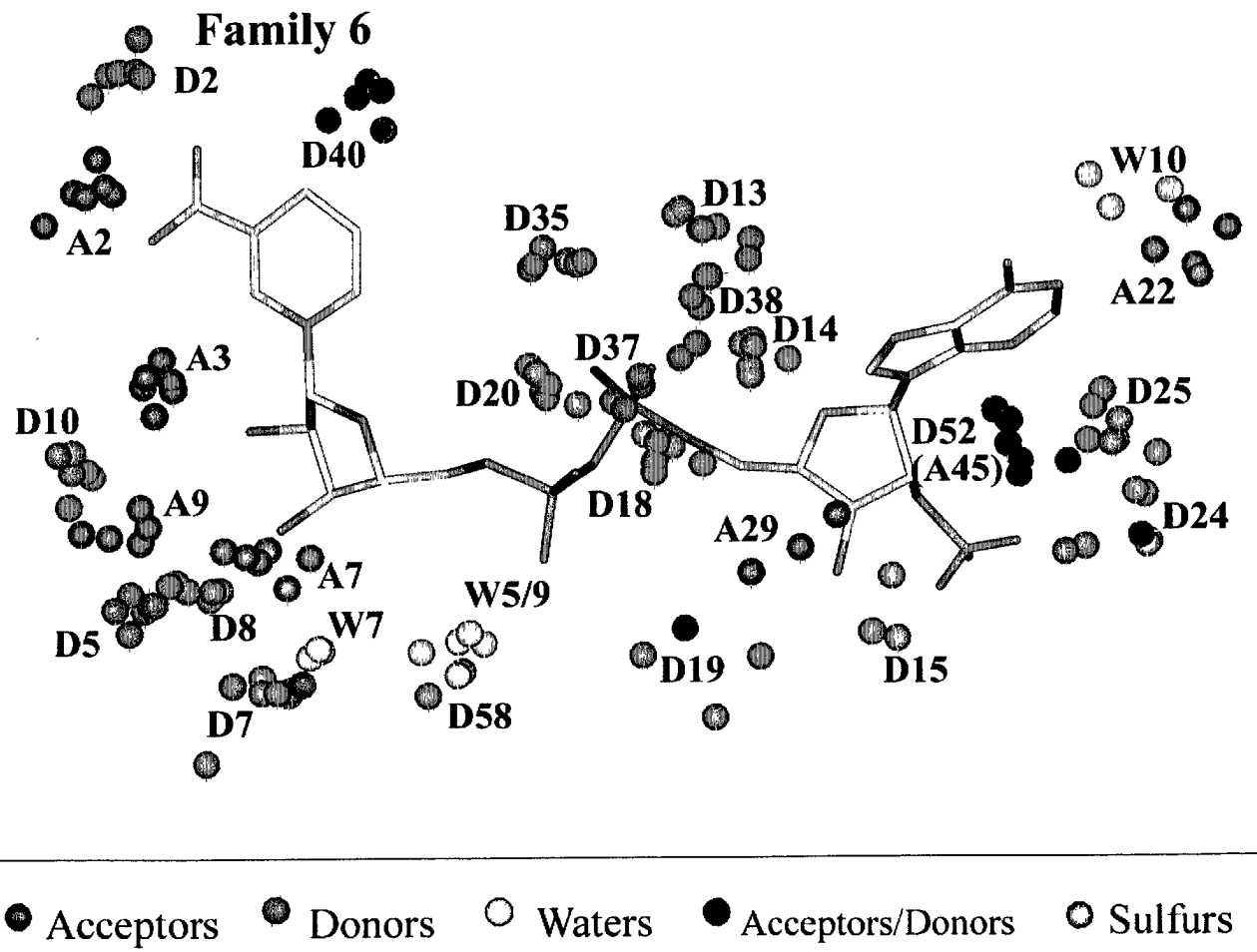
T08227 S680h00t



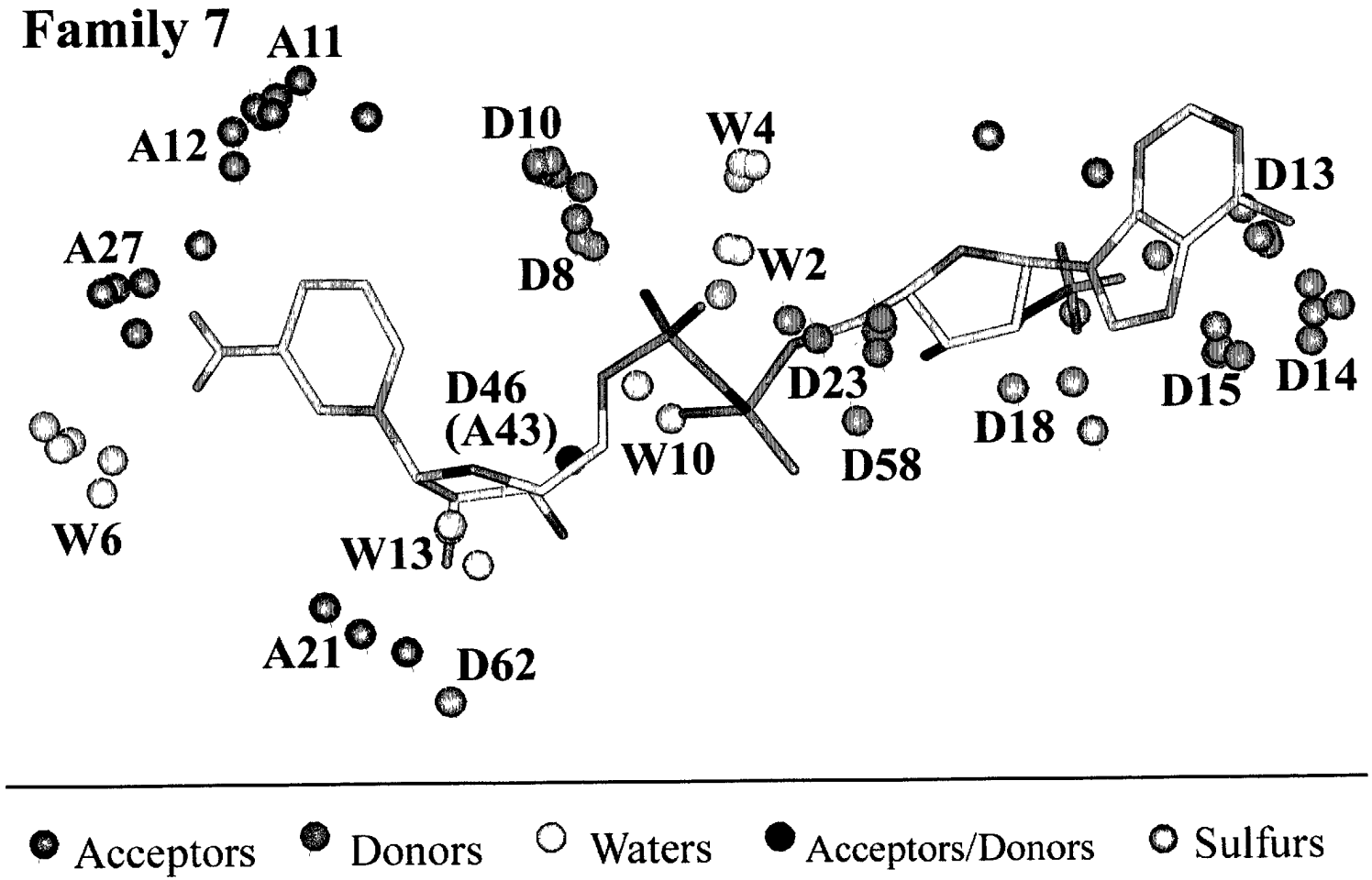
TOP27T 5820-H00T

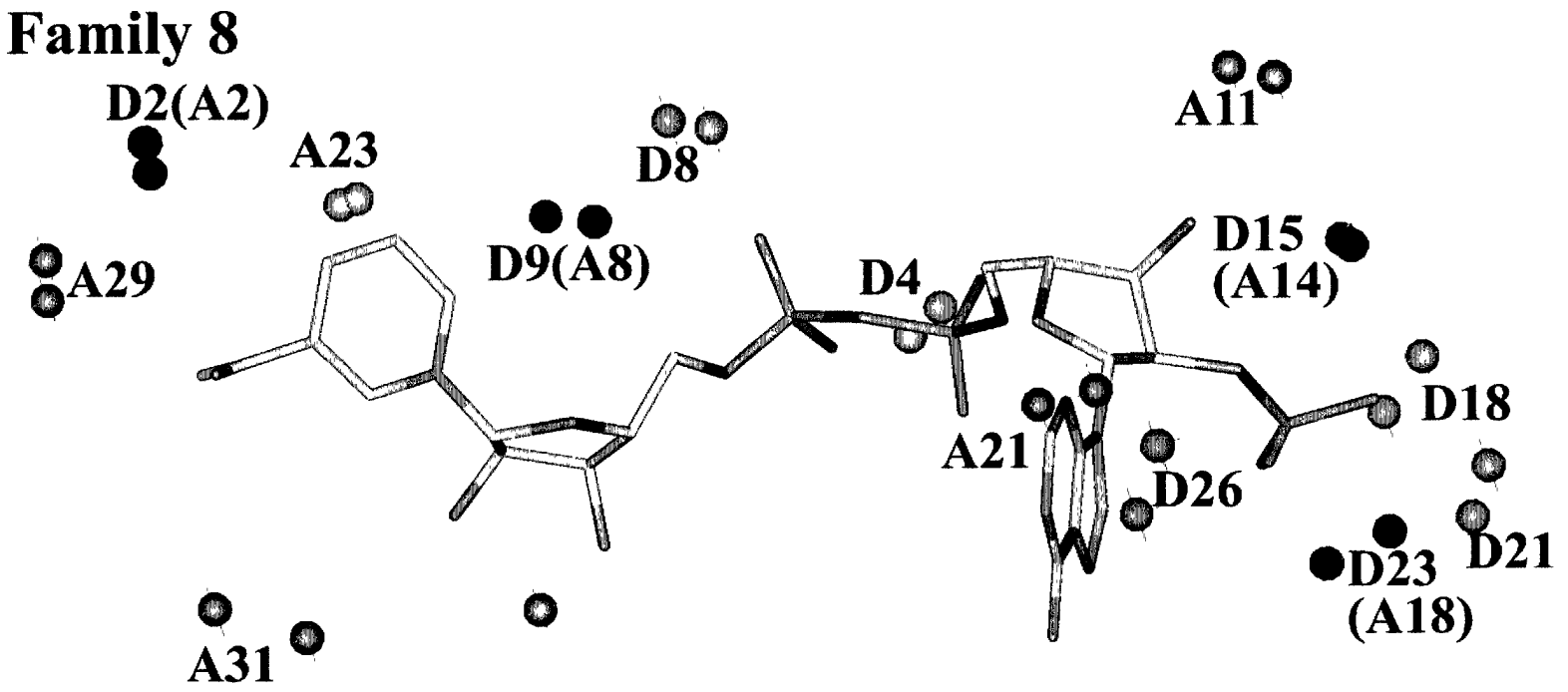


T09227 S680h001



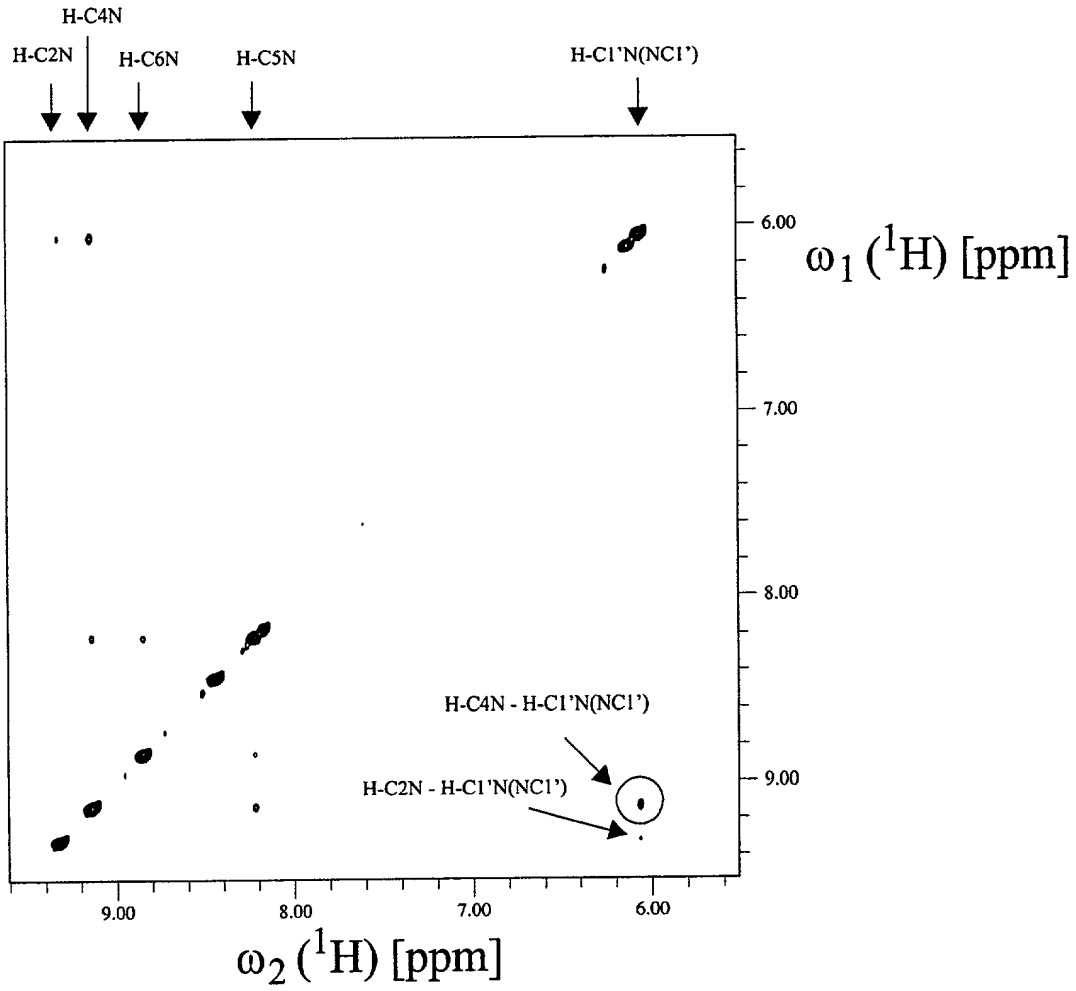
Sem et al.
P-TB 5072
Figure 3F


Family 7
A11
A12
A27
D10
D8
W4
W2
D13
D14
D15
D18
D23
D58
D46
(A43)
W10
W6
W13
A21
D62
Acceptors
Donors
Waters
Acceptors/Donors
Sulfurs

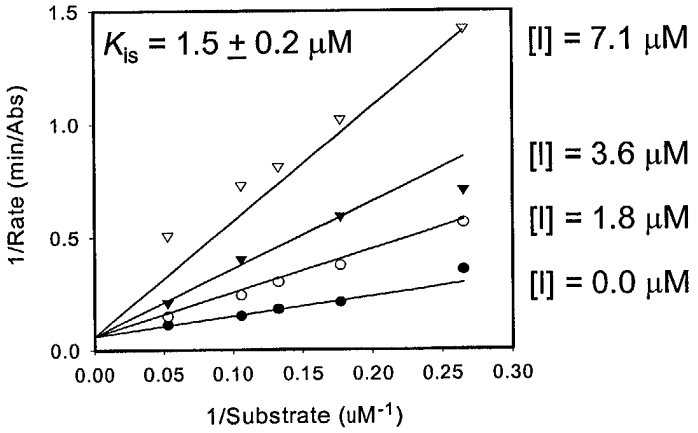


Sem et al.
P-TB 5072
Figure 3H

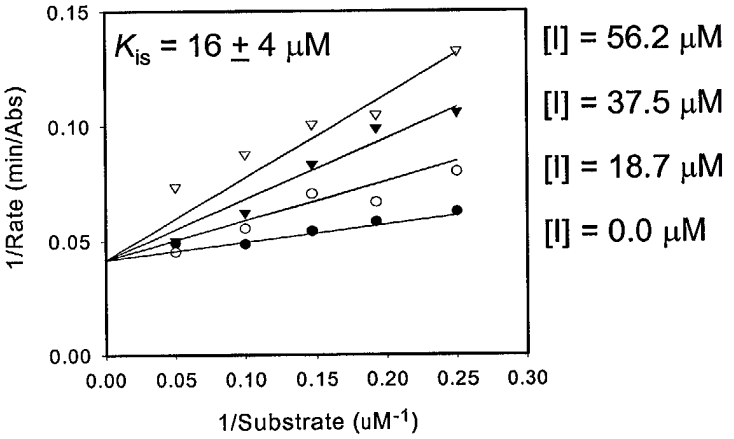
Sem et al.
P-TB 5072
Figure 4



A.
Compound: TTE0001.001.A7
Pharmacofamily 1 examplar



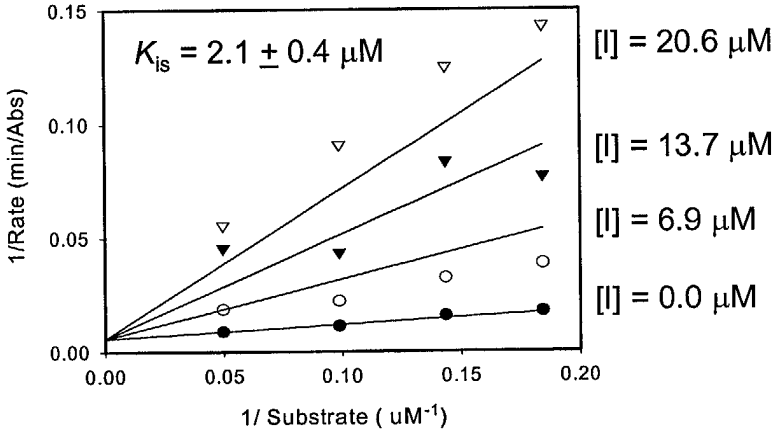
B.
Compound: TTE0001.001.A7
Pharmacofamily 8 examplar



Sem et al.
P-TB 5072
Figure 5

T0827T "5680h007

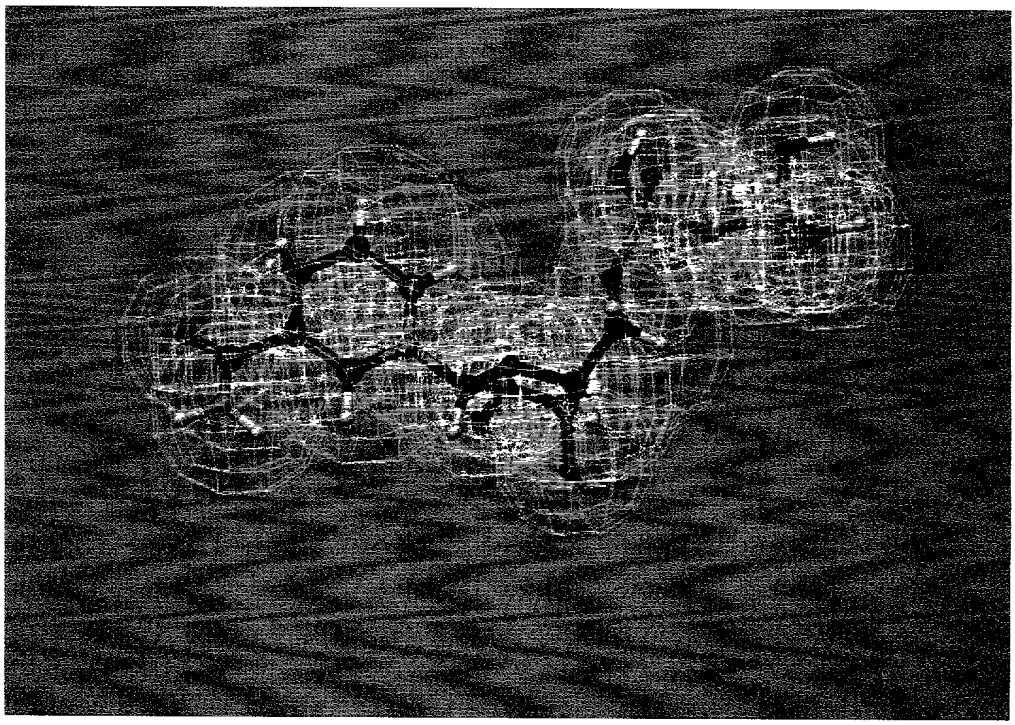
A.
Compound: TTE0001.002.D2
Pharmacofamily 1 examplar



B.
Compound: TTE0001.002.D2
Pharmacofamily 8 examplar

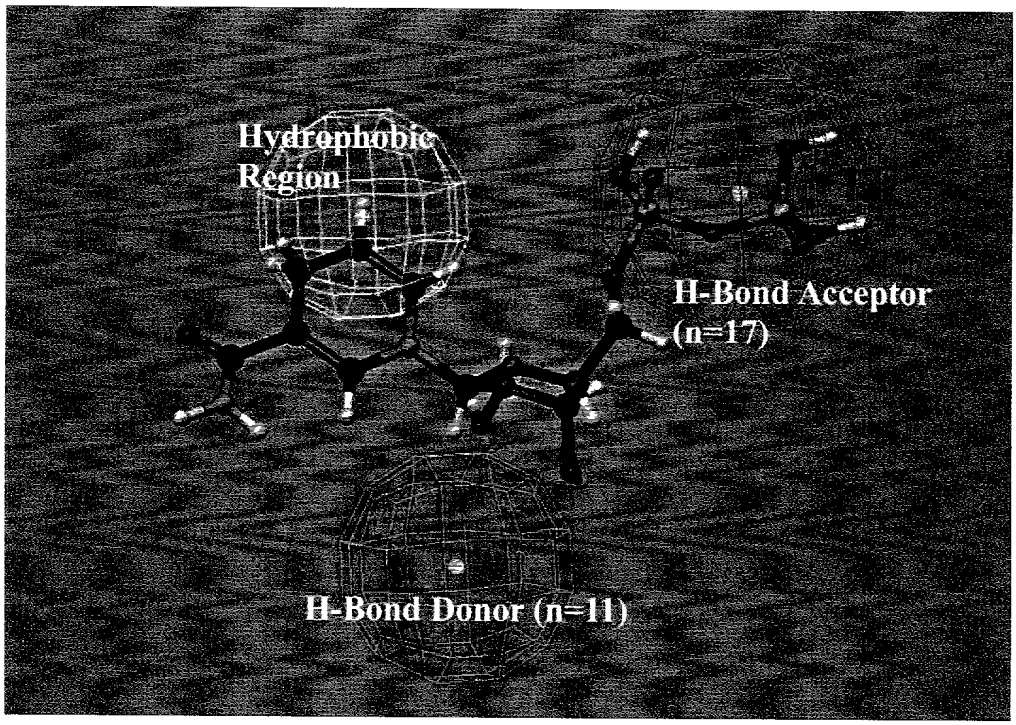
K_{is} > 1 mM

Sem et al.
P-TB 5072
Figure 7A

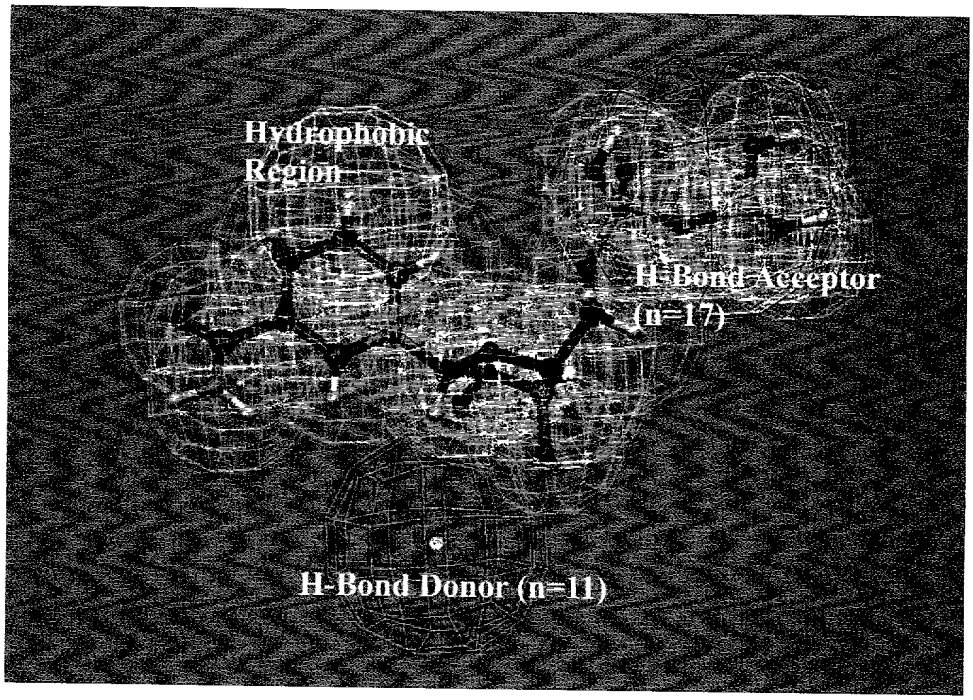


Approved - Unclassified

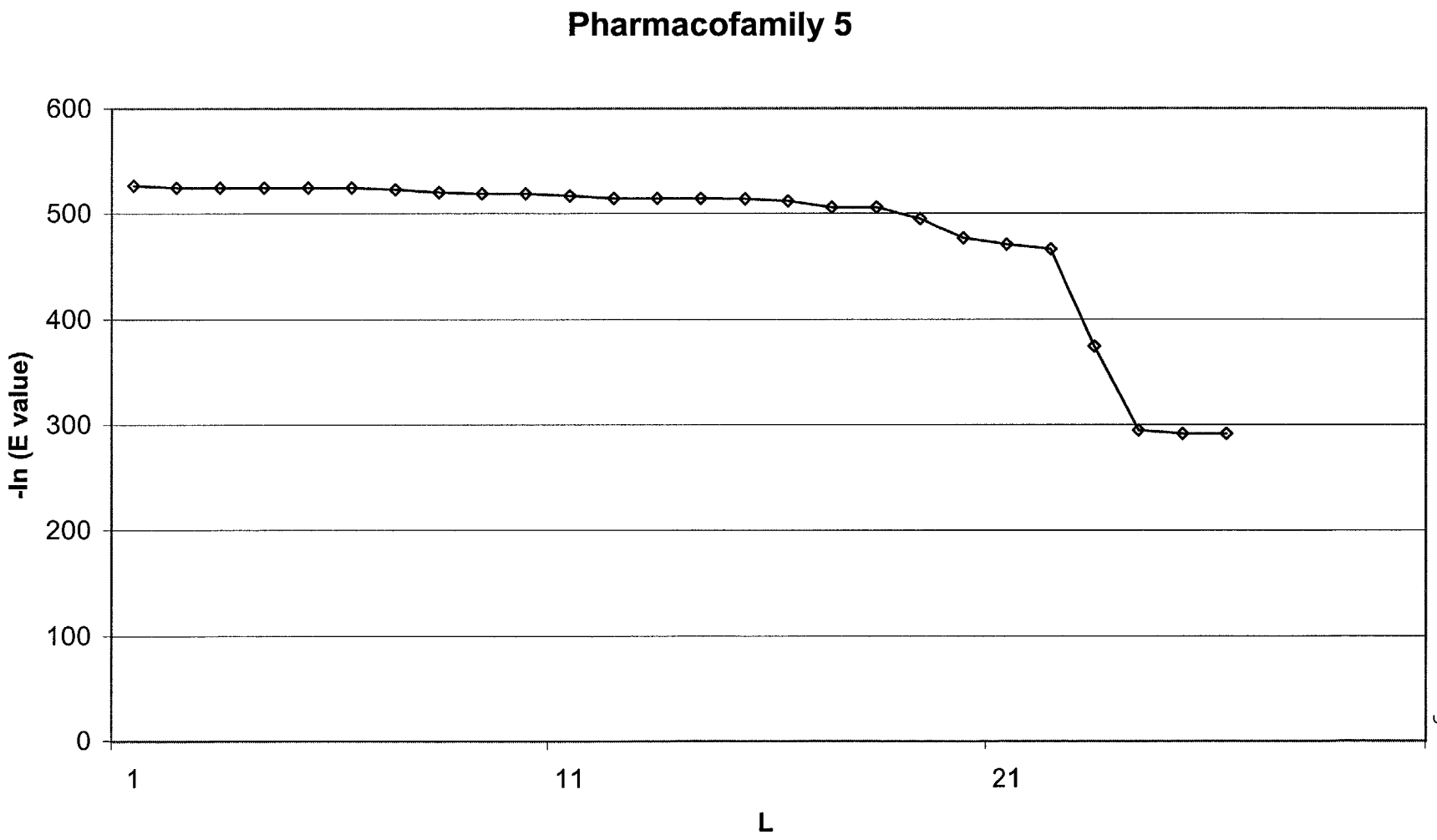
Sem et al.
P-TB 5072
Figure 7B



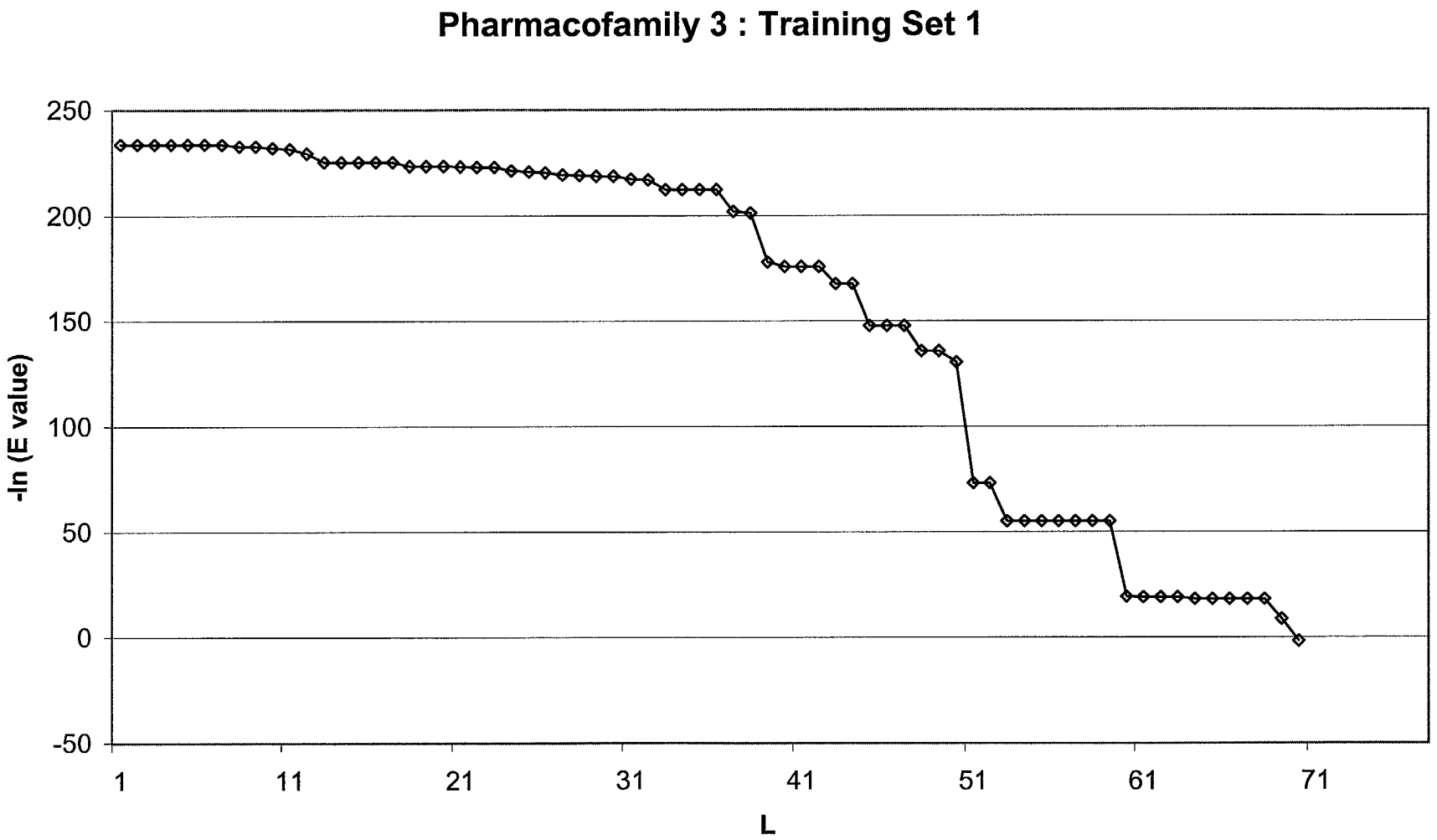
Sem et al.
P-TB 5072
Figure 7C



Page 1 of 1 - 5072 - 1/1/2004

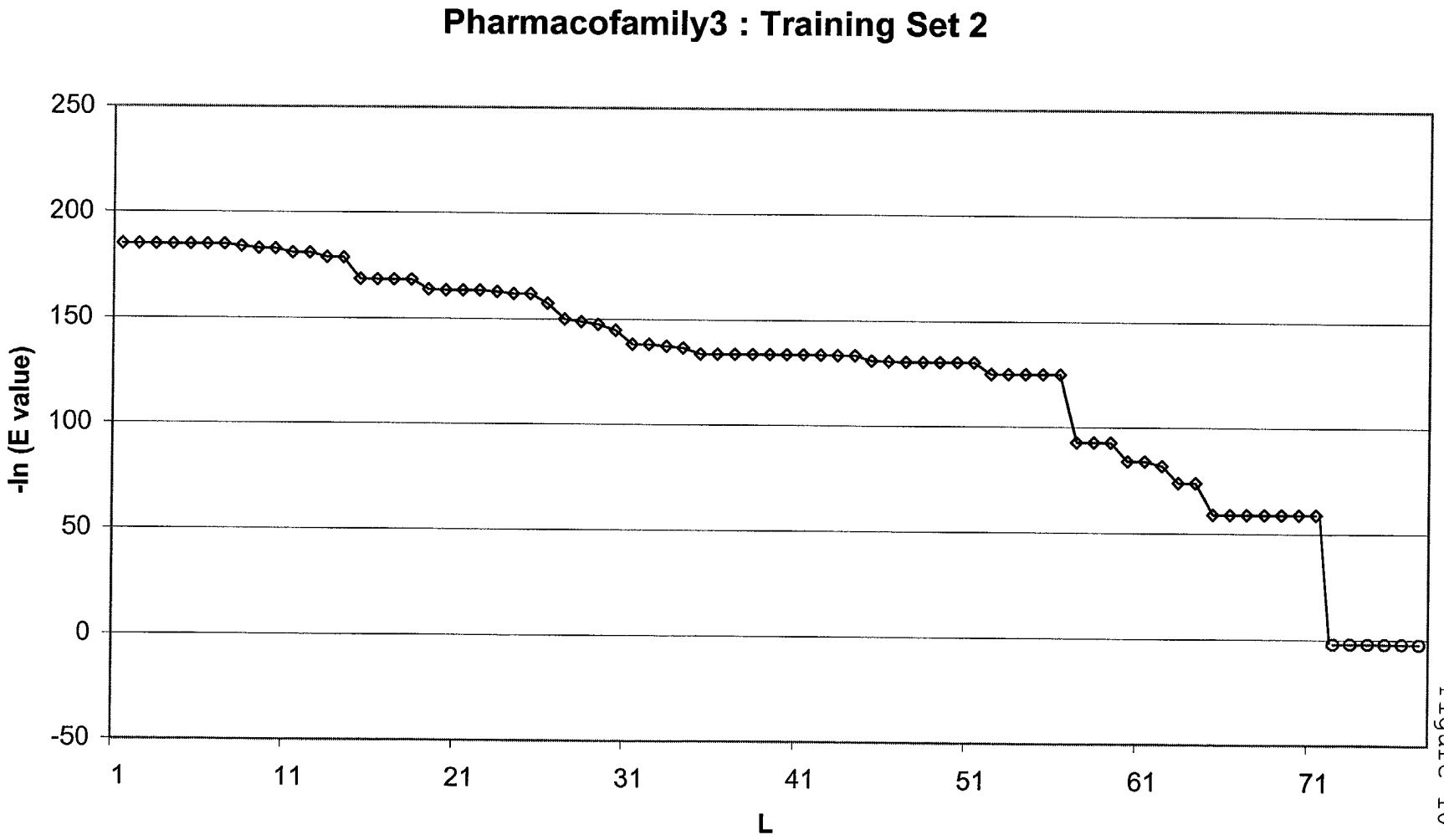


Sem et al.
P-TB 5072
Figure 8



Sem et al.
P-TB 5072
Figure 9

T03227 "S680h00T



Sem et al.
P-TB 5072
Figure 10

```
refinement cycle   5
profile center:1AGN
profile length:  599
1AGN
1AXE
1YKF
1HYH
1LDN
1EMD
9LDB
4MDH
1BMD
1PSD
1DXY
2NAD
1A4I
1B3R
1PJC
1ARZ
1QR6

1AGN:  .......... .CL....... ......IGC. .GFSTGYGAA VKTGK...V.
1AXE:  .......... .......... .......GC. .GFSTGYGSA VKVAK...V.
1YKF:  .......... .VM....... ......IPD. .MMTTGFHGA E.LAD...I.
1HYH:  .......... .......... .......... .......... ..........
1LDN:  .......... .......... .......... .......... ..........
1EMD:  .......... .......... .......... .......... ..........
9LDB:  .......... .......... .......... ..ATLKDQL. I.HNL...L.
4MDH:  .......... .......... .......... .......... ..........
1BMD:  .......... .......... .......... .......... ..........
1PSD:  .....P.... ..F....... .......SN. .TRSVAELV. IGELL.LLLR
1DXY:  ...SNV.... ..P....... ......AYS. .PAAIAEFA. LTDTL.YLLR
2NAD:  .......... .......... .......CN. .SISVAEHV. VMMIL.SLVR
1A4I:  .......... .......... .......... ..PCTPKGC. LELIK.ET.G
1B3R:  .......... .......... ......KFD. NLYGCRESL. IDGIKRAT.D
1PJC:  .......... .......... .......TPM SI.IAGRLSV Q.FGA.RFLE
1ARZ:  .......... .......... .......... .......... ..........
1QR6:  LIQFEDFGNH NAFRFLRKYR EKYCTFNDD. .IQGTAAVA. LAGLL.AAQK

1AGN:  .......... .......... .......... ...KP..... .G.STCVVF.
1AXE:  .......... .......... .......... ...TQ..... .G.STCAVF.
1YKF:  .......... .......... .......... ...EL..... .G.ATVAVL.
1HYH:  .......... .......... .......... .......... .A.RKIGIIG
1LDN:  .......... .......... .......... ....MK..NN GG.ARVVVIG
1EMD:  .......... .......... .......... .......... ...MKVAVLG
9LDB:  .......... .......... .......... ..KEE...HV PH.NKITVVG
4MDH:  .......... .......... .......... ...SE..... .P.IRVLVTG
1BMD:  .......... .......... .......... ..MKA..... .P.VRVAVTG
1PSD:  ..GVPEANAK A..HRGV.W. NKL..AA.G. SFEAR..... .G.KKLGII.
1DXY:  ..NMGKVQAQ L..QAGDYEK AGT..F..I. GKELG..... .Q.QTVGVM.
2NAD:  ..NYLPSHE. WARK.GGWN. .IADCVSHA. Y.DLE..... .A.MHVGTV.
1A4I:  .......... .......... .......... .VPIA..... .G.RHAVVV.
1B3R:  .......... .......... .......... .VMIA..... .G.KVAVVA.
1PJC:  RQQ....... .......... .......GGR GVLLGGVPGV KP.GKVVIL.
1ARZ:  .......... .......... .......... ....N..... ...IRVAIAG
1QR6:  ..V....... .......... ........I. SKP.I..... .SEHKILFL.
```

```
1AGN:  GLGG.VGLSV IMGCK..SA. ......G... .A.SRIIGID ..L.N.....
1AXE:  GLGG.VGLSV IMGCK..AA. ......G... .A.ARIIGVD ..I.N.....
1YKF:  GIGP.VGLMA VAGAK..LR. ......G... .A.GRIIAVG ....S.....
1HYH:  L.GN.VGAAV AHGLIAQGV. .A........ .D..DYVFID A.N.E.....
1LDN:  A.GF.VGASY VFALMNQGI. .A........ .D..EIVLID A.N.E.....
1EMD:  AAGG.IGQAL ALLLKTQLP. ..S...G... .S..ELSLYD I.A.P.....
9LDB:  V.GA.VGMAC AISILMKEL. .A........ .D..EIALVD V.M.E.....
4MDH:  AAGQ.IAYSL LYSIG.NG.S VFGKDQP... .I..ILVLLD ITP.MM....
1BMD:  AAGQ.IGYSL LFRIA.AG.E MLGKDQP... .V..ILQLLE I.PQAM....
1PSD:  GYGH.IGTQL GILAE..SL. ......G... .M..YVYFYD I...E.....
1DXY:  GTGH.IGQVA IKLFK..GF. ......G... .A..KVIAYD P...Y.....
2NAD:  AAGR.IGLAV LRRLA..PF. ......D... .V..HLHYTD ....R.....
1A4I:  GRSKIVGAPM HDLLL..WN. ......N... .A..TVTTCH S...K.....
1B3R:  GYGD.VGKGC AQALR..GF. ......G... .A..RVIITE I...D.....
1PJC:  GGGV.VGTEA AKMAV..GL. ......G... .A..QVQIFD I...N.....
1ARZ:  AGGR.MGRQL IQAAL.ALE. GV........ .Q..LGAALE REG.SS....
1QR6:  GAGE.AALGI ANLI...VS. ..VENGLSEQ EAQKKIW.FD K...YGLLVK

1AGN:  ...KD.KFEK AM.AVGA... .......... .......... .T.E.C...I
1AXE:  ...KD.KFAK AK.EVGA... .......... .......... .T.E.C...V
1YKF:  ...RPVCVDA AK.YYGA... .......... .......... .T.D.I...V
1HYH:  ...A..KVK. .A.D.QID.. FQ.....DAM ANL.EAH.G. NI.V.I...N
1LDN:  ...S..KAI. .G.D.AMD.. FN.....HGK V.FAPKP.V. DI.W.H...G
1EMD:  ...V...TP. .G.V.AVD.. LS.....HI. ..P..TA.V. KI.K.G...F
9LDB:  ...D..KLK. .G.E.MMD.. LQ.....HGS L.F..LR.TP KI.V.S...G
4MDH:  ...G..VLD. .G.V.LME.. L......QDC ..A..LPLLK DV.I.A...T
1BMD:  ...K..ALE. .G.V.VME.. LE.....DCA .....FPLLA GL.E.A...T
1PSD:  ...N..K... .L...P.... LG........ .......... NA.T.Q...V
1DXY:  ......P... .M.K.GD... HP........ .......... DF.D.Y...V
2NAD:  ...H..R... .L.P..ES.. VE.......K .....E..L. NL.T.W...H
1A4I:  .......... .......... .......... .......... ..........
1B3R:  ...PI.NAL. .Q.A.AM... EG........ .......... .Y.E.V...T
1PJC:  ...VERL... .SYL..ETL. FG.......S .......... RV.ELL...Y
1ARZ:  ...L...LG. .S.D.A.... GELAGAGK.T .......... GV.T.V...Q
1QR6:  GRKAK..... .I.D...SYQ EP........ .......... .FTHSAPESI

1AGN:  S...PKDSTK PI.S.EVLSE M.T..G.NNV GYTFEVIG.. ...H......
1AXE:  N...PQDYKK PI.Q.EVLTE M.S..N.GGV DFSFEVIG.. ...R......
1YKF:  N...YKDG.. PI.E.SQIMN L.T..EGKGV DAAIIAGG.. ...N......
1HYH:  ....D..... ...W....A. .ALAD....A DVVISTLG.. ...NIKLQQ.
1LDN:  ....D..... ...Y....D. .DCRD....A DLVVICAG.. ...AN..QKP
1EMD:  SGE.D..... .A.T.PAL.. ..E.G....A DVVLISAG.. ...VR..RK.
9LDB:  K...D..... ...Y.NVT.. ..A.N....S RLVVITAG.. ...AR..QQE
4MDH:  D...K..... .EEI..AFK. ..D......L DVAILVGS.. ...MP..RR.
1BMD:  D.D.P..... .D.V..AFK. ..D......A DYALLVGA.. ...AP.RKA.
1PSD:  Q.H.L..... .S.D..LLN. ..M......S DVVSLHVPEN .PST......
1DXY:  S...L..... .E.D..LFK. ..Q......S DVIDLHVPGI .EQN......
2NAD:  AT..R..... .E.D..MYP. ..V......C DVVTLNCPLH .PET......
1A4I:  TAH.L..... .D.E..EVN. ..K......G DILVVATG.. ...Q......
1B3R:  T...M..... .D.E..ACK. ..E......G NIFVTTTG.. ...C......
1PJC:  SNSAE..... IE.T..AVA. ..E......A DLLIGAVLVP GRRA......
1ARZ:  S...S..... ...LDAV.K. ..D.D....F DVFIDFT... ...R......
1QR6:  PDT.F..... ED.A...VN. ILK......P STIIGVAGA. ...G......
```

PCT/US99/14950

```
1AGN:  .......... ...L...ETM .I.DALA.SC ....HMNYGT SVVVGV..P.
1AXE:  .......... ...L...DTM .V.TALS.CC ....QEAYGV SVIVGV..P.
1YKF:  .......... ...A...DIM .A.TAVK.IV .....KPGGT IANVNY..F.
1HYH:  .....FA..E LKFTSSMV.Q S..V.GTNLK .ESGFH..GV LVVISN.P..
1LDN:  GET.RLD..L VDKNIAIF.R S..I.VESVM .ASGFQ..GL FLVATN.P..
1EMD:  PGMDRSD..L FNVNAGIV.K N..L.VQQVA .KT.CP.KAC IGIITN.P..
9LDB:  G.ESRLN..L VQRNVNIF.K F..I.IPNIV .KY.SP.NCK LLVVSN.P..
4MDH:  DGMERKDL.L .KANVKIF.K C..Q.GAALD .KY.AKKSVK VIVVGN.P..
1BMD:  .GM..ERRDL LQVNGKIF.T E..Q.GRALA .EV.AKKDVK VLVVGN.P..
1PSD:  .......... ...K..NM.M GAKE.ISLM. ....KP.GSL LINASR.GT.
1DXY:  .......... ...T..HI.I NEAA.FNLM. ....KP.GAI VINTAR.PN.
2NAD:  .......... ...E..HM.I NDET.LKLF. ....KR.GAY IVNTAR.GK.
1A4I:  .......... ...P..EM.V ...K.GEWI. ....KP.GAI VIDCGI..N.
1B3R:  .......... ...V...DII ...L.GRHFE .Q..MKDDAI VCNIGH.F..
1PJC:  .......... ...P...I.L ...VPASLVE .Q..MRTGSV IVDVAV.DQ.
1ARZ:  .......... ...P..EGTL N..H.LAFCR .Q..HG..KG MVIGTT..G.
1QR6:  .......... ...R...L.F TPDV.IR..A AS..INERPV IFALSNPTAQ

1AGN:  .PSA.K.M.. .L.TY.D.PM .......... .L....L... ......FT..
1AXE:  .PDS.Q.N.. .L.SM.N.PM .......... .L....L... ......LS..
1YKF:  .GE..GEV.. ...L....PV .......PRL EWGC..G... ......MA..
1HYH:  .....V.D.. .V.I..TALF .....QHV.. .......... ......TG..
1LDN:  .....V.D.. .I.L..TYAT .....WKF.. .......... ......SG..
1EMD:  .....V.N.. .T.T..VAIA .....AEV.. .......... ......LKKA
9LDB:  .....V.D.. .I.L..TYVA .....WKI.. .......... ......SG..
4MDH:  .....A.N.. .T.N..CLTA .....SKS.. .......... ......AP..
1BMD:  .....A.N.. .T.N..ALIA .....YKN.. .......... ......AP..
1PSD:  .V...V.D.. .I.PA.LCDA .......... .L....A... ......SK..
1DXY:  .L...I.D.. .T.QA.MLSN .......... .L....K... ......SG..
2NAD:  .L...C.D.. .R.DA.VARA .......... .L....E... ......SG..
1A4I:  ..YKVV.G.. .D.VA.YD.E .....A.... .K....E... ..........
1B3R:  .....D.V.. .E.ID.VKW. .....LNEN. ...AVEKVNI KPQVDRYL..
1PJC:  .......G.. .GCVETLHPT SHTQPTY... .E....V... ..........
1ARZ:  .....F.DEA GK.QA.IRDA .......... .A........ ......AD..
1QR6:  AE...C.... .TAEE.AYTL .......... ......T... ......E...

1AGN:  ......GR.T WK......GC .......... .......... ..........
1AXE:  ......GR.T WK......GA .......... .......... ..........
1YKF:  ......HK.T IK......GG .......... .......... ..........
1HYH:  .....FPAHK VI..G...TG ....T..... .......... ..........
1LDN:  .....LPHER VI..G...S. .......... .......... ..........
1EMD:  GV...YDKNK LF..G...VT ........TL DI...IRSNT FVAEL..KGK
9LDB:  .....FPKNR VI..G...SG ....C...N. .......... ..........
4MDH:  .S...IPKEN FS..C...LT ........RL DH...NRAKA QIALK..LGV
1BMD:  .G...LNPRN FT..A...MT ........R. .......... ..........
1PSD:  .....H.LAG AA......ID VFPTE...P. .ATNSD.... .PF.T..S..
1DXY:  .....K.LAG VG......ID TYEYETEDL. .LN..LAKH. GSFKDPLW.D
2NAD:  .....R.LAG YA......GD VWFPQ...P. .A........ .PK.D..H..
1A4I:  .....R.ASF IT..PVPGGV ....G...P. .......... ..........
1B3R:  .LKNGHRI.I LLAEG...RL V...N...L. .......... ..........
1PJC:  .....FGV.V HY..G...VP .......... .......... ..........
1ARZ:  ........I.A IV..F...A. A...N..... .......... ..........
1QR6:  .......GRC LF..A...SG SP..F..... .......... .......G.P
```

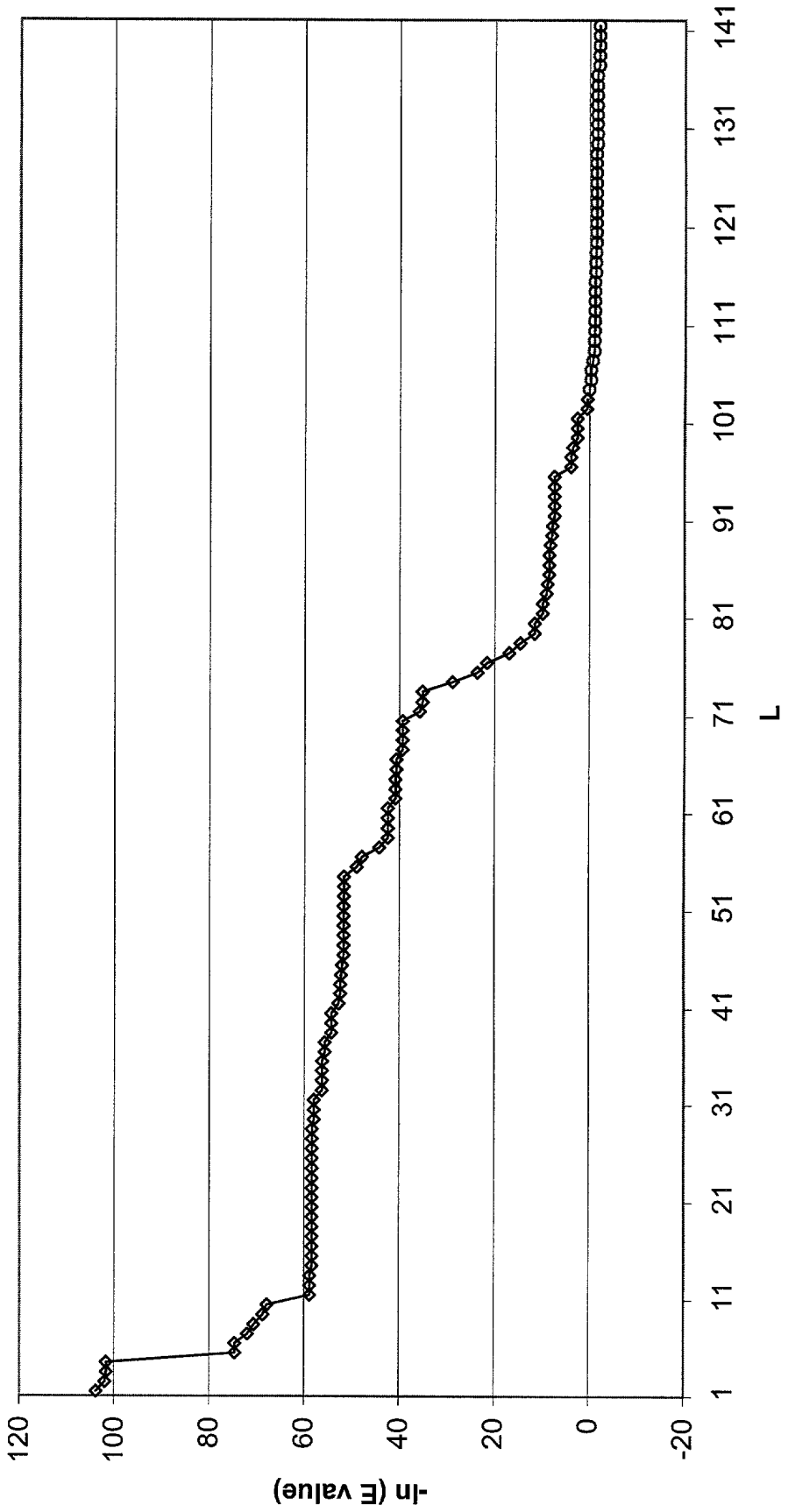
PCT/US99/14804

```
1AGN:  .......... ........V. FGG.L...KS .......... ..........
1AXE:  .......... ........I. FGG.F...KS .......... ..........
1YKF:  .......... ........L. C...P...GG ..RLRME... R.LIDL....
1HYH:  .......... .......... .......... .......... ..........
1LDN:  .......... .......... .......... .......... ..........
1EMD:  QPGE....VE V.PVIG.GHS G.V.TI..LP LLS.QVPG.. ...V....SF
9LDB:  .......... .......... .......... .......... ..........
4MDH:  TS.D....DV KNVIIWGNHS S.T.Q...YP DVNHAKVKLQ AKEVGVYEAV
1BMD:  .......... .........LD .......... .......... ..........
1PSD:  .P.L....CE FDNVLLTPHI G.G.S...TQ EAQENI.... ..........
1DXY:  .E.L....LG MPNVVLSPHI A.Y.Y...TE TAVHNMV... Y.FSLQ....
2NAD:  .P.W....RT MPYNGMTPHI S.G.T..... .......... ..........
1A4I:  .......... ........M. TVA.M...LM .Q..S..... ..........
1B3R:  .......... ......G.C. A.MGH...PS FV........ ..........
1PJC:  .......... ........NM PGA.VPWTA. .......... ..........
1ARZ:  .......... .......F.. S.V.G...A. .S..S..... ..........
1QR6:  .V.KLTDGRV F..TPGQGN. NVY.I...FP GVALAVILCN TRHISD....

1AGN:  .......... .......... .......... .......... ..........
1AXE:  .......... .......... .......... .......... ..........
1YKF:  .......... .......... .......... ...V..FYKR VDPS.K.L..
1HYH:  .......... .......... .......... .......... ..........
1LDN:  .......... .......... .......... .......... ..........
1EMD:  T.E.QEV.AD LTKRIQNAGT EVVEAKAGGG SATLSMGQAA ARFGLS.LVR
9LDB:  .......... .......... .......... .......... ..........
4MDH:  KDDSW.LKGE FITTVQQRGA AVIKARK..L SSAMSAAKAI CDHV.RDI..
1BMD:  .......... .......... .......... .......... ..........
1PSD:  .......... .......... .......... .......... ..........
1DXY:  .......... H.LVDFLTKG ETSTEVTG.. .......... ..........
2NAD:  .......... .......... .......... .......... ..........
1A4I:  .......... .......... .......... .......... ..........
1B3R:  .......... .......... .......... .......... ..........
1PJC:  .......... .......... .......... .......... ..........
1ARZ:  .......... .......... .......... ...R..MTFA NGAV.RSAL.
1QR6:  .......... .......... .......... ...S..VFLE AA...KA...

1AGN:  .......... .......... .......... .......... ..........
1AXE:  .......... .......... .......... .......... ..........
1YKF:  ........V. .......... .......... .......... ..........
1HYH:  .......... .......... .......... .......... ..........
1LDN:  .......... .......... .......... .......... ..........
1EMD:  A.LQGEQGVV .....ECAYV EG.DG..QYA ..RFFS.QPL LLGKNGVEER
9LDB:  .......... .......... .......... .......... ..........
4MDH:  W....F..GT PEGEFVSMGI ISDGNSYGVP DDLLYSFPVT IKD..KT.WK
1BMD:  .......... .......... .......... .......... ..........
1PSD:  .......... .......... .......... .......... ..........
1DXY:  .......... .......... .......... .......... ..........
2NAD:  .......... .......... .......... .......... ..........
1A4I:  .......... .......... .......... .......... ..........
1B3R:  .......... .......... .......... .......... ..........
1PJC:  .......... .......... .......... .......... ..........
1ARZ:  WLSGKESGLF ....DMR... .......... ........D. ..........
1QR6:  ........LT S..QLTD... .......... .......EEL .........A
```

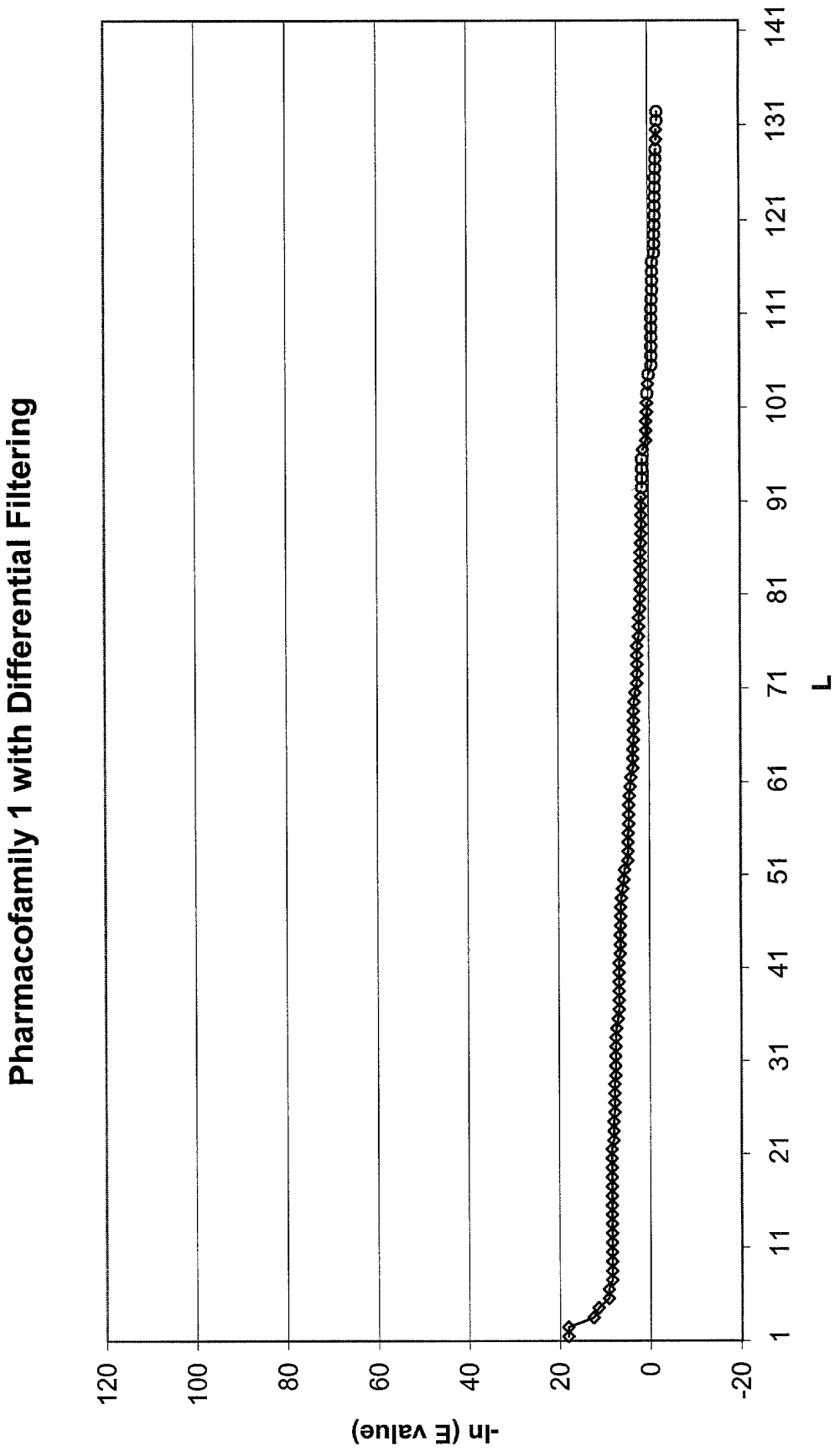
1100405 - 1102501

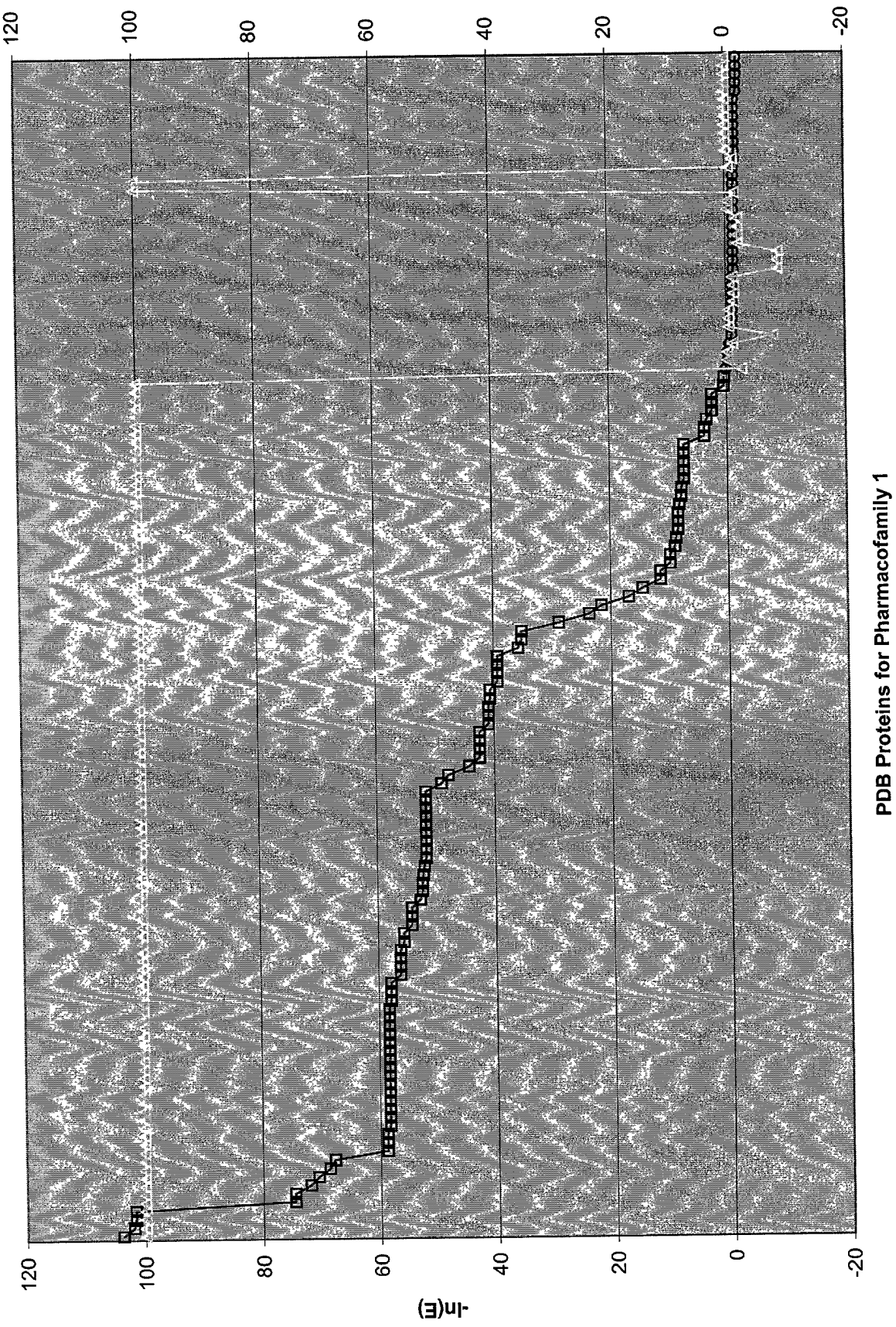
```
1AGN:  .......... .......... .......... .......... ..........
1AXE:  .......... .......... .......... .......... ..........
1YKF:  .......... .......... .......... .......... ..........
1HYH:  .......... .......... .......... .......... ..........
1LDN:  .......... .......... .......... .......... ..........
1EMD:  K.S....I.G TLSAFEQNAL EG.ML...DT LKK.DIALGQ EF..VNK..
9LDB:  .......... .......... .......... .......... ..........
4MDH:  I.V....EGL PI.N..DFS. REKMDLTAKE L.AEE..KET AFEFL.SSA
1BMD:  .......... .......... .......... .......... ..........
1PSD:  .......... .......... .......... .......... ..........
1DXY:  .......... .......... .......... .......... ..........
2NAD:  .......... .......... .......... .......... ..........
1A4I:  .......... .......... .......... .......... ..........
1B3R:  .......... .......... .......... .......... ..........
1PJC:  .......... .......... .......... .......... ..........
1ARZ:  ...VLDLN.N L......... .......... .......... ..........
1QR6:  QGRLYPPL.A NIQE.VSINI AIKVTEYLYA NKAFRYPEPE DKAKYVKER
```

1QR6.ALN - 1QR6:1



Patent Application Publication


Pharmacofamily 1 with Differential Filtering
-ln (E value)
120
100
80
60
40
20
0
-20
1
11
21
31
41
51
61
71
81
91
101
111
121
131
141
L


XCorr for pharmacofamily 1
-ln(E)
120
100
80
60
40
20
0
-20
PDB Proteins for Pharmacofamily 1